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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Mark R. Prausnitz, Jin Liu, and Thomas N. Lewis

Serial No.: 09/229,226

Art Unit: 3737

Filed: January 12, 1999

Examiner: R. Smith

For: *ASSESSMENT AND CONTROL OF ACOUSTIC TISSUE EFFECTS*

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF

Sir:

This is a Brief in reply to the Examiner's Answer mailed May 19, 2003 in the above-identified patent application. A Request for Oral Hearing accompanies this Reply Brief. The Commissioner is hereby authorized to charge \$140, the fee for a Request for Oral Hearing for a small entity, to Deposit Account No. 50-1868. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

(6) ISSUES ON APPEAL

The issues presented on appeal are:

- (1) whether claims 1-25 and 27-33 are clear and definite as required by 35 U.S.C. § 112, second paragraph;
- (2) whether claims 1-2, 10, 11, 14, 15, 17, 19, 21, and 23-28 were properly rejected under 35 U.S.C. § 102(e) as lacking novelty over U.S. Patent No. 6,113,559 to Klopotek ("Klopotek");

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(3) whether claims 27, 28 and 30 were properly rejected under 35 U.S.C. § 102(b) as lacking novelty over U.S. Patent No. 5,445,611 to Eppstein, et al. ("Eppstein");

(4) whether claim 22 was properly rejected under 35 U.S.C. § 103(a) as obvious over Klopotek;

(5) whether claim 26 was properly rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,636,632 to Bommannan, et al. ("Bommannan") in view of Klopotek;

(6) whether claims 1-5, 8-18, 23-26, and 29 were properly rejected under 35 U.S.C. § 103(a) as obvious over Eppstein in view of Klopotek;

(7) whether claims 1-3, 5, 7, 14, 15, 18, 23, and 25-27 were properly rejected under 35 U.S.C. § 103(a) as obvious over Tachibana, et al. *Cancer Lett* 72(3): 195-199 (1993) ("Tachibana") in view of Klopotek; and

(8) whether claim 6 was properly rejected under 35 U.S.C. § 103(a) as obvious over Eppstein in view of Bommannan.

(8) ARGUMENTS

Appellants affirm all of the arguments made in the Appeal Brief.

The Examiner's Answer states that the statement of the issues is correct in the Appeal Brief, but did not include U.S. Patent No. 5,656,016 to Ogden in the list of the prior art of record nor in the list of rejections under 35 U.S.C. § 103. Therefore, it appears that the rejection of claim 26 under 35 U.S.C. § 103(a) over Ogden in view of Klopotek has been overcome by Appellants' arguments in the Appeal Brief.

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(b) Rejections Under 35 U.S.C. § 112, second paragraph

Claims 31-33 depend from claim 27 and further define the locations that the transducer is placed. These claims are directed to application of ultrasound using invasive or minimally invasive means (see e.g. claim 31). The specification teaches that non-invasive, minimally invasive, or invasive methods can be used to apply the acoustic energy (see page 11, lines 17-17). Claim 32 specifies using a catheter, which is a minimally invasive method. Claim 33 describes a surgical incision, which is generally viewed as an invasive method. For example, a surgeon could place the transducer within the abdominal cavity to deliver ultrasound to a more remote site, such as the retroperitoneal space (e.g. kidneys, duodenum, pancreas, etc.). Therefore the methods defined by claims 31-33 require applying a transducer at one site and treat an internal organ, internal tissue or internal vessel on a tissue with acoustic energy at a second site that is distant from the first site, as defined by claim 27. Thus claims 31-33 further define the method of claim 27 and are definite.

(c) Rejections Under 35 U.S.C. § 102

Claim 27

Claim 27 defines a method for altering cell viability or transport of chemical or biological agents into or through an internal organ, internal tissue or vessel in a human or other animal using acoustic energy. It requires the step of administering acoustic energy at one or more frequencies by applying a transducer to a first site, which is not the location where transport or cell viability is to be altered. Claim 27 specifies that the acoustic energy is effective to alter transport or cell viability at a second site that is distant from the first site and is a different tissue,

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internal organ or internal vessel in a different tissue. Thus, based on the requirement in the preamble, the second site must be an internal organ, an internal tissue, or an internal vessel on an internal tissue.

Klopotek

Klopotek discloses applying ultrasound to the skin to reduce wrinkles in the skin. Klopotek teaches that the ultrasound energy triggers a biological response in the dermis (see col. 1, lines 59-61). Contrary to the Examiner's assertion, the dermis is not an internal organ nor is it an internal tissue. The dermis is layer within an external tissue, the skin. Therefore, Klopotek does not anticipate claims 1, 2, 10, 11, 14, 15, 17, 19, 21, and 23-28, which require the presence of an effect from the ultrasound application on an internal organ or internal tissue.

Eppstein

Like, Klopotek, Eppstein is limited to examining the effects of ultrasound within the skin. Column 9, lines 33-46 disclose that ultrasound, when applied to the skin's surface, provides access to layers of tissue beneath the stratum corneum, such as the epidermis and dermis. Nowhere does Eppstein teach that any remotely located internal tissues or internal organs are affected by the application of ultrasound to the surface of the skin. Therefore, claims 27, 28 and 30 are novel in view of Eppstein.

(d) Rejections Under 35 U.S.C. § 103

Tachibana in view of Klopotek

Tachibana discloses applying low frequency ultrasound directly to cells in combination with a photoactive cytotoxic agent (*Photofrin II*) to kill cells. Tachibana teaches that the

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ultrasound produces free radicals which induce a cytotoxic effect in the drug, resulting in an increase in the amount of cells killed. Nowhere does Tachibana teach applying ultrasound to one location to produce an effect in a second distant location. Further, Tachibana does not teach that the ultrasound is used to aid in drug delivery to cells.

Klopotek and Tachibana are directed at different methods. Klopotek is directed at reducing wrinkles in skin, while Tachibana is directed at killing cells. Klopotek teaches that the ultrasound should be applied at a frequency and intensity that induces hypothermia (i.e. increases the temperature in the skin) or cavitation (see col. 3, lines 32-37). In contrast, Tachibana is directed at the application of low level, non-thermal ultrasound, which is not described as inducing cavitation (see page 198). Therefore, different types of ultrasound are applied in these different methods. There is no teaching or suggestion to combine Klopotek with Tachibana. Therefore, one of ordinary skill in the art would not combine Klopotek with Tachibana.

Further, even if one of ordinary skill in the art did combine the teachings of Klopotek with those of Tachibana, claims 1-3, 5, 7, 14, 15, 18, 23, and 25-27 would not be obvious for the reasons stated in the Appeal Brief.